

The following listing of the claims shall replace all previous listings of the claims in this application.

1. (currently amended) An antibody ~~fragment comprising a~~ Fab' fragment that has been modified by attachment of at least one effector molecule wherein the heavy chain in the fragment is not covalently bonded to the light chain, and both the interchain cysteine of C<sub>L</sub> and the interchain cysteine of C<sub>H1</sub> have been replaced with another amino acid, and wherein said at least one effector molecule is a 5,000 to 40,000 KDa PEG or a PEG derivative thereof that is an  $\alpha$ -halocarboxylic acid or ester, an imide, a vinyl sulphone, ~~or~~ a disulphide or a maleimide, wherein the hinge region contains one or two cysteines, and wherein the hinge region is optionally modified.
2. (currently amended) The antibody Fab' fragment of claim 1 wherein the interchain cysteine of C<sub>L</sub> and the interchain cysteine of C<sub>H1</sub> have been replaced with a non-thiol containing amino acid.
3. (currently amended) The antibody Fab' fragment of claim 2 wherein the interchain cysteine of C<sub>L</sub> has been replaced with serine.
4. (currently amended) The antibody Fab' fragment of claim 2 wherein the interchain cysteine of C<sub>H1</sub> has been replaced with serine.
5. (currently amended) The antibody Fab' fragment of claim 2 wherein both the interchain cysteine of C<sub>H1</sub> and the interchain cysteine of C<sub>L</sub> have been replaced with serine.
6. (currently amended) The antibody Fab' fragment of claim 1 wherein the interchain cysteine of C<sub>L</sub> is at position 214 of the light chain and the interchain cysteine of C<sub>H1</sub> is at position 233 of the heavy chain.
7. (currently amended) The antibody Fab' fragment of claim 1 wherein at least one

effector molecule is attached to the heavy or light chain constant region of the fragment.

8. (currently amended) The antibody Fab' fragment of claim 1 wherein an effector molecule is attached to an engineered cysteine in the light chain constant region and to an engineered cysteine in the heavy chain constant region of the fragment.

9. (currently amended) The antibody Fab' fragment of claim 8, wherein the cysteine residues in the heavy and light chain constant regions which are attached to effector molecules would otherwise be linked to each other via a disulphide bond if the effector molecules were not attached.

10. (currently amended) The antibody Fab' fragment of claim 1 wherein the fragment is a Fab' fragment that contains a modified hinge region.

11. (previously presented) The antibody fragment of claim 10 wherein the modified hinge region contains 1 cysteine residue.

12. (previously presented) The antibody fragment of claim 11 wherein the modified hinge region comprises the sequence of SEQ ID NO:1 or SEQ ID NO:2.

13. (previously presented) The antibody fragment of claim 10 wherein the modified hinge region contains 2 cysteine residues.

14. (previously presented) The antibody fragment of claim 10 wherein the modified hinge region comprises the sequence of SEQ ID NO:3 or SEQ ID NO:4.

15. (previously presented) The antibody fragment of claim 1 wherein the fragment is a Fab' fragment in which at least one effector molecule is attached to the hinge region of the fragment.

16. (previously presented) The antibody fragment of claim 15 in which two effector

molecules are attached to the hinge region of the fragment.

17. (previously presented) The antibody fragment of claim 1 wherein the fragment is a Fab' fragment in which each effector molecule attached to the fragment is attached to the hinge region of the fragment.

18. (previously presented) The antibody fragment of claim 1 in which the fragment is a Fab' fragment in which each effector molecule attached to the fragment is attached to a cysteine in the hinge region of the fragment.

19. (withdrawn) A method of producing an antibody Fab or Fab' fragment to which at least one effector molecule is attached comprising: a. treating an antibody Fab or Fab' fragment in which both the interchain cysteine of C<sub>L</sub> and the interchain cysteine of C<sub>H1</sub> have been replaced with another amino acid with a reducing agent capable of generating at least one free thiol group in the fragment; and b. reacting the treated fragment with an effector molecule.

20. (withdrawn) The method of claim 19 wherein the reducing agent is a non-thiol based reducing agent.

21. (withdrawn) The method of claim 20 wherein the reducing agent is a trialkylphosphine.

22. (withdrawn) The method of claim 21 wherein the trialkylphosphine reducing agent is tris(2-carboxyethyl)phosphine (TCEP).

23. (withdrawn) The method of claim 21 wherein the trialkylphosphine reducing agent is tris(3-hydroxypropyl)phosphine (THP).

24. (withdrawn) The method of claim 19 wherein either or both of steps (a) and (b) are performed in the presence of a chelating agent.

25. (withdrawn) The method of claim 24 wherein the chelating agent is EDTA.
26. (withdrawn) The method of claim 25 wherein both steps (a) and (b) are performed in the presence of EDTA.
27. (Canceled)
28. (Canceled)
29. (previously presented) The antibody fragment of claim 1 wherein each effector molecule is PEG.
30. (previously presented) A pharmaceutical composition comprising an antibody fragment of claim 1, together with one or more pharmaceutically acceptable excipients, diluents, or carriers.